

The University of Chicago

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A DISSERTATION SUBMITTED TO THE
FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY
FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY

DEPARTMENT OF CHEMISTRY
1938

By
WILLARD R. SPROWLS

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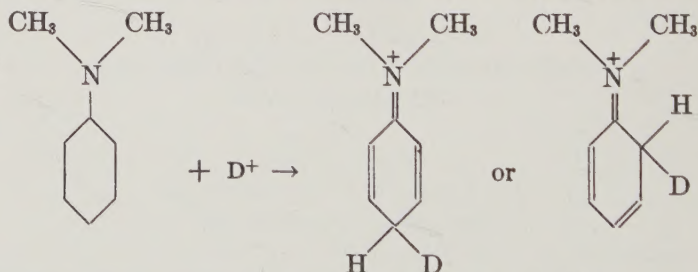
EXCHANGE REACTIONS IN DEUTEROALCOHOL. II.

W. R. SPROWLS

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In the first paper of¹ this series we reported the results of a preliminary investigation of hydrogen-deuterium exchange reactions involving organic substances of various types and deuteroalcohol as the solvent and donor of deuterium. The experiments included representatives of two different types of exchange reaction which could be differentiated on the basis of catalytic influences. One class comprises the base-catalyzed exchange reactions of substances of inherent acidic properties, such as fluorene, *o*- and *p*-nitrotoluene, and sym-trinitrobenzene. The second type of exchange reaction exhibits acid catalysis, as in the case of dimethylaniline,* and, since the reaction is initiated by acids, the lability of hydrogen is clearly a consequence of the molecule having functioned as a base. The survey has been continued in various directions, but with particular emphasis on reactions of the second type, that is, the acid-catalyzed exchange reactions of dimethylaniline and related substances.

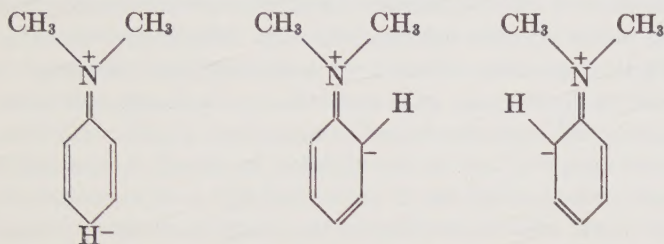
The mechanism of the dimethylaniline exchange reaction was briefly discussed in our first paper and it was pointed out that while the normal reaction of dimethylaniline with a dilute acid would be the formation of an ammonium salt, this salt would not necessarily be an intermediate in the exchange reaction. In fact, having in mind the deactivating effect of salt formation in nuclear substitution reactions, mechanisms involving the normal ammonium salt as an intermediate seemed somewhat less probable than one involving the direct addition of protons at the nuclear positions, giving rise to tautomeric forms of the salt, as follows:



¹ KHARASCH, BROWN, AND McNAB, *J. Org. Chem.*, **2**, 36 (1937).

* The acid-catalyzed hydrogen exchange reaction of dimethylaniline in aqueous

This mechanism is suggested by the interpretation of the structure of the free base as a resonance hybrid of the normal aromatic resonance forms together with three zwitterion forms shown below:



The free base is to be regarded, of course, as a single composite structure, but the fact that the pair of electrons normally available for salt formation on the nitrogen atoms may be shared with the two ortho positions and the para position makes more plausible the assumption that the molecule may accept a proton at any one of these points. The products formed would no longer be resonance forms but tautomeric forms, and it will be evident that dissociation of the quinoid forms of the salt, but not of the normal form, will give rise to hydrogen exchange.

The two hypotheses would seem to be experimentally distinguishable if the influence of base strength on the ease of hydrogen exchange is considered. If the normal ammonium salt is an intermediate in the exchange reaction, then structural changes which decrease the basicity of the molecule should also inhibit the exchange reaction. If, however, the structural change decreases the basic strength mainly by increasing the number or the stability of the zwitterion resonance forms, and if the salts derived from these forms are the intermediates, the exchange reaction should be facilitated. Thus we should expect triphenylamine to be capable of exchanging hydrogen at a rate of about the same order of magnitude as for dimethylaniline, despite the tremendous disparity in base strength, since the effect of substituting phenyl groups for methyl groups will be to increase the number of resonance structures and so to increase the number of points at which a proton may become attached.

The experimental results which have been obtained for a number of substances in this category are, on the whole, in accord with the hypothesis that quinoid forms of the salts act as intermediates. Unfortunately, rate

solution was reported prior to the publication of our first paper by INGOLD, RAISIN, AND WILSON (*J. Chem. Soc.*, **1936**, 1636), who also supposed that the reaction is limited to the ortho and parahydrogens. These authors were also the first to consider a mechanism of direct introduction of deuterium into the aromatic nucleus, and the mechanism which was given in our first paper (Ref. 1, p. 43, footnote) should be credited to them. It will be noted, however, that the mechanism proposed in the present paper presents a number of distinctly new features.

data which could be handled in rigorous kinetic fashion are not yet readily available, as the experimental procedure is still too cumbersome, and with our present methods rate studies would be too costly in materials.

The behavior of dimethylaniline has been carefully re-investigated in view of the rather peculiar results which were reported previously. Those results, while they demonstrated an acid-catalyzed exchange reaction involving three hydrogens, indicated also an exchange reaction to the extent of about 0.5 hydrogen in both neutral and alkaline solution. Since this reaction appeared not to be inhibited by alkali, it was felt that the experimental results must be in error, perhaps as a consequence of the presence of some dimethylaniline in the samples of alcohol which were analyzed for deuterium. It is now found, after repeating the experiments and exercising greater care in the separation of the mixtures, that dimethylaniline does not exchange hydrogen appreciably in the absence of acid. This result has been checked repeatedly.

Diphenylamine exchanges one hydrogen, presumably the *N*-hydrogen, in the absence of acid, while in the presence of acid the exchange number rises to six. The most probable value for the number of exchangeable hydrogen atoms, consistent with the value of six for the exchange number, is seven, and it is therefore likely that the exchange reaction in the presence of acid involves the ortho and para positions in each ring in addition to the hydrogen attached to nitrogen. Triphenylamine behaves similarly, the observed exchange number, 7.9, corresponding to the exchange of nine hydrogens. There is, therefore, no marked diminution in the ability of the nuclear hydrogens to exchange which would parallel the very great decrease in basicity in the series, dimethylaniline, diphenylamine, and triphenylamine, and these results provide convincing evidence against the normal salt (or ion) as an intermediate in the exchange reaction.

The nitro derivatives of dimethylaniline exhibit very striking differences in the lability of the nuclear hydrogens. The theoretical limit for the number of exchangeable hydrogens, assuming that only the hydrogens ortho and para to the dimethylamino group are labile, would be two for *o*- and *p*-nitrodimehtylaniline, and three for the meta compound. Actually the ortho compound exhibits no exchange at all under the experimental conditions we have adopted. The hydrogen exchange of the para compound under the influence of acid is practically complete, and the exchange of the meta compound under the same conditions, while greater in absolute amount than for the para compound, falls short of the theoretical limit, and the meta compound is therefore to be regarded as intermediate in reactivity.

The failure of *o*-nitrodimehtylaniline to exchange is to be correlated

with the observations² that this compound does not form a nitroso derivative with nitrous acid, does not couple with diazo compounds, and does not condense with aldehydes as is characteristic not only of dimethylaniline itself but also of *m*-nitrodimethylaniline. The deactivating effect is not however specific for the nitro group; dimethyl-*o*-toluidine³ and *o*-chlorodimethylaniline² likewise fail to react with nitrous acid and to couple with diazonium salts, and it has been postulated by Karrer⁴ that the effect is due to steric hindrance. Because of these effects, Karrer was led to suppose that the initial point of attack by the reagent in coupling and nitrosation reactions is the nitrogen atom, which in turn necessitates a rearrangement to obtain the final product.

In the present instance, at least, it would not appear to be necessary to assume that the initial point of attack is the nitrogen atom in order to see how steric effects might arise. Both the orthoquinoid and the paraquinoid forms of the aryltrimethylammonium salts, which in our hypothesis act as intermediates in the exchange reactions, will possess a configuration such that the methyl groups are confined to the plane of the ring as a consequence, based on classical theory, of the presence of the nitrogen-carbon double bond. The steric effect of an ortho substituent could then consist in a tendency to prevent the alkyl groups from assuming this configuration, the result of which would be to increase the energy of activation required for the formation of the reaction intermediate which is now a form of higher energy (lower stability). Since the contribution to the activation energy arising from this source need be relatively small in order to account for the observed results, it is by no means necessary to assume that rotation of the dialkylamino group is entirely prevented or that the hindrance would necessarily be sufficient to introduce optical isomerism in the case where the dialkylamino group is unsymmetrical. Otherwise the type of optical isomerism discovered by Mills and Kelham⁵ in the case of *N*-acetyl-*N*-methyl-*p*-toluidine-3-sulfonic acid would be more commonly encountered. An effect amounting to between five and ten kilocalories in the energy of activation would appear to be sufficient to account for the phenomenon, little more, for example, than the estimated energy of rotation about the C—C bond in ethylene chloride. An interaction energy of this magnitude in the present instances appears not to be unreasonable, but that it could be of such significance for the chemistry of the substance is at first sight surprising.

² FRIEDLÄNDER, *Monatsh.*, **19**, 638 (1898).

³ WURSTER AND RIEDEL, *Ber.*, **12**, 1796 (1879).

⁴ KARRER, *ibid.*, **48**, 1398 (1915).

⁵ MILLS AND KELHAM, *J. Chem. Soc.*, **1937**, 274.

The steric effect which we suppose to originate in the tautomeric forms of the dimethylaniline salts is in certain respects similar to, and is probably supplemented by, an effect manifesting itself in the free base which is known as damped resonance. The effect is similar in that the quinoid resonance forms of the free base, from which the tautomeric forms of the cation may be considered as derived, are rendered less stable by the presence of an ortho substituent, which tends to prevent a planar arrangement, with the result that these forms contribute less to the actual structure of the molecule. This idea was introduced by Birtles and Hampson⁶ who believed that the abnormally large dipole moment of *p*-nitrodimethylaniline is due to the contribution of a quinoid resonance form and who predicted correctly that the substitution of four methyl groups in the nuclear positions would restore the dipole moment to a normal value. Further evidence has been accumulating rapidly. The effect of damped resonance in the free base will be to decrease the enhancement of nuclear reactivity which has its origin in resonance involving the nitrogen atom, and, insofar as exchange reactions are concerned, will be indistinguishable from the analogous steric effects in the cation forms. However, there appears to be a possibility of securing independent experimental evidence for the effect of damped resonance in molecules of the type under consideration in an examination of the relative base strengths of ortho and para isomers; the effect should be manifested by an increase in the base strength of the ortho isomer.*

It is our belief that the essential ideas underlying this interpretation of the exchange reactions can be extended profitably to other reactions in which ortho effects appear, and we are therefore continuing the investigation not only with the aid of exchange reactions but with regard to some other types of substitution as well. However, in suggesting that this type of steric hindrance is of general significance in connection with ortho effects in nuclear substitutions, we do so while recognizing that in indi-

⁶ BIRTLES AND HAMPSON, *ibid.*, 1937, 10. Since this article was submitted for publication a second paper, which deals with chemical applications of the principle of damped resonance has appeared [INGHAM AND HAMPSON, *J. Chem. Soc.*, 1939, 981.]

* Since this paper was written our attention has been drawn to the fact that there are several known instances in which the base strength of ortho-substituted tertiary bases is greater than that of the corresponding meta- and para-substituted bases, whereas, in accordance with the interpretation on the basis of damped resonance, no such ortho effect manifests itself in the base strength of primary and secondary amines [for experimental data, see DAVIES AND ADDIS, *J. Chem. Soc.*, 1937, 1622; WALKER, *Z. phys. Chem.*, 57, 608 (1906)]. Further manifestations of the effect of damped resonance are to be seen in the refractivities and ultraviolet absorption spectra of ortho-substituted tertiary bases as will be shown more fully in a subsequent paper.

vidual cases the purely steric factor may be only one of several factors influencing nuclear reactivity and that in special circumstances it may be altogether absent.

The alkali-catalyzed exchange reaction of the hydrocarbon, fluorene, is representative of a distinctly different type of hydrogen lability, namely, a type in which the labile hydrogen is acidic. That fluorene is readily capable of reacting as a proton donor is well known from its condensation reactions and the formation of salts with the alkali metals, and its strength as an acid has been determined by Conant and Wheland⁷. The fact that triphenylmethane, which is also capable of salt formation, did not exchange hydrogen under the same experimental conditions is in accord with the relative positions of fluorene and triphenylmethane in the acidity series established by these authors. Further evidence for the existence of a relationship between the ability of such substances to exchange hydrogen and their acid strength was provided by Heuse⁸ who showed that xanthane, which occupies an intermediate position in the acidity series, is also intermediate in its rate of hydrogen exchange. He found also that indene and 9-phenylfluorene, which, according to Conant and Wheland, are both somewhat stronger as acids than fluorene, exhibited hydrogen exchange under the influence of alkali at least as readily as fluorene.

It is clearly evident from these results that the origin of the extraordinary lability of hydrogen in indene and in fluorene derivatives is to be sought in the cyclopentadiene nucleus, and we may note, as others have done, that the formation of an anion by the loss of a proton would convert the cyclopentadiene nucleus to a structure in which various possibilities for resonance are present. The stabilization effect of resonance in the anion would result in a lowering of the energy of electrolytic dissociation and thus in an increase in acid strength. The assumption of such electronic mobility in the anions seems necessary also in order to account for rearrangements of a prototropic type which occur when certain indene derivatives are treated with alkali. In the case of indene itself we could predict the exchange of three hydrogens under the influence of alkali if we are to assume a resonating anion as an intermediate. This anion would certainly be electronically symmetrical about the *beta* carbon atom, and in the reformation of the indene molecule by proton capture, the incoming proton could enter at either alpha position. The repetition of the processes of dissociation and recombination would then give rise ultimately to the exchange of three hydrogens. Heuse, in his work on the exchange of indene catalyzed by sodium hydroxide, obtained values for the exchange

⁷ CONANT AND WHELAND, *J. Am. Chem. Soc.*, **54**, 1212 (1932).

⁸ HEUSE, Master's Dissertation, University of Chicago, 1937.

TABLE I
EXCHANGE REACTIONS OF DIMETHYLANILINE AND RELATED SUBSTANCES

REF. NO.	SUBSTANCE	MMOL. SUB- STANCE	MMOL. ALCOHOL	CATALYST	TEMP., °C.	TIME, HRS.	INITIAL D ₂ O	FINAL D ₂ O	EXCHANGE NUMBER
1	Dimethylaniline	39.3	85.8	—	110	96	3.43	3.35	0.06
4	Dimethylaniline	39.3	85.8	—	110	96	3.43	3.35	0.06
80	Dimethylaniline	39.3	85.8	—	110	112	3.17	3.06	0.08
12	Dimethylaniline	39.3	85.8	NaOH, 2 mg.	110	137	3.43	3.37	0.04
2	Dimethylaniline	39.3	85.8	H ₂ SO ₄ , 140 mg.	110	96	3.43	1.56	2.55
41	Dimethylaniline	39.3	85.8	H ₂ SO ₄ , 140 mg.	25	24	3.10	2.97	0.13
7	Diphenylamine	29.6	85.8	—	110	115	3.43	2.47	1.13
14	Diphenylamine	29.6	85.8	NaOH, 2 mg.	110	115	3.43	2.46	1.14
10	Diphenylamine	29.6	85.8	H ₂ SO ₄ , 140 gm.	110	96	3.43	1.12	5.98
17	Triphenylmethane	20.4	85.8	—	110	98	3.43	3.36	0.09
22	Triphenylmethane	20.4	85.8	NaOH, 2 mg.	110	115	3.43	3.41	0.03
19	Triphenylmethane	20.4	85.8	H ₂ SO ₄ , 140 mg.	110	105	3.43	1.19	7.93
37	Triphenylmethane	8.2	85.8	H ₂ SO ₄ , 100 mg.	25	115	3.10	3.07	
28	<i>p</i> -Nitrodimethylaniline	9.1	85.8	—	110	101	3.10	3.09	0.03
27	<i>p</i> -Nitrodimethylaniline	9.7	85.8	NaOH, 2 mg.	110	97	3.10	3.08	0.06
26	<i>p</i> -Nitrodimethylaniline	12.0	85.8	H ₂ SO ₄ , 100 mg.	110	96	3.10	2.48	1.62
35	<i>p</i> -Nitrodimethylaniline	12.0	85.8	—	110	96	3.10	3.08	0.04
34	<i>m</i> -Nitrodimethylaniline	12.0	85.8	NaOH, 2 mg.	110	96	3.10	3.07	0.07
33	<i>m</i> -Nitrodimethylaniline	12.0	85.8	H ₂ SO ₄ , 100 mg.	110	96	3.10	2.44	2.08
54	<i>m</i> -Bromodimethylaniline	6.8	85.8	—	110	120	3.10	2.75	1.21
75	<i>m</i> -Bromodimethylaniline	6.8	85.8	—	110	98	3.17	2.99	0.76
53	<i>m</i> -Bromodimethylaniline	13.7	85.8	NaOH, 2 mg.	110	96	3.10	3.06	0.08
49	<i>m</i> -Bromodimethylaniline	13.7	85.8	H ₂ SO ₄ , 100 mg.	110	96	3.10	2.20	2.41
92	<i>o</i> -Nitrodimethylaniline	27.6	85.8	—	110	111	3.17	3.22	
94	<i>o</i> -Nitrodimethylaniline	27.6	85.8	NaOH, 2 mg.	110	98	3.17	3.20	
98	<i>o</i> -Nitrodimethylaniline	27.6	85.8	H ₂ SO ₄ , 140 mg.	110	99	3.17	2.86	0.24

TABLE II
EXCHANGE REACTIONS OF FLUORENE AND RELATED SUBSTANCES

REF. NO.	SUBSTANCE	M- MOLES.	CATALYST	TEMP., °C.	TIME, HRS.	INITIAL D ₂ O	FINAL D ₂ O	EX- CHANGE NUM- BER	REMARKS
3	Fluorene	30.1	NaOH, 2 mg.	110	69	3.43	2.16	1.70	2 H's exchange
40	9-Fluorenel	8.8	—	110	108	3.10	2.80	1.12	Exchange of OH hydrogen
38	9-Fluorenel	9.4	NaOH, 2 mg.	110	96	3.10	2.58	1.84	2 H's exchange
76	9-Fluorenel	9.1	NaOH, 1 mg.	25	1226	3.17	2.80	1.25	Exchange of 2nd H incomplete
93	9-Fluorenel	11.0	NaOH, 439 mg.	25	12	3.17	2.69		Decomposition
83	9-Fluorenel	4.2	Na ₂ CO ₃ , 450 mg.	25	43	3.17	2.84	1.19	
39	9-Fluorenel	9.6	H ₂ SO ₄ , 100 mg.	110	119	3.10			Decomposition
77	9-Methoxyfluorene	15.3	—	110	95	3.17	3.14	0.05	No exchange
78	9-Methoxyfluorene	15.3	NaOH, 2 mg.	110	116	3.17	3.15	0.04	No exchange
79	9-Methoxyfluorene	15.3	H ₂ SO ₄ , 100 mg.	110	116	3.17	3.03		Decomposition
57	9-Amino fluorene	8.3		110	96	3.10	2.58		Decomposition
58	9-Amino fluorene	11.0	NaOH, 2 mg.	110	115	3.10	2.30		Decomposition
59	9-Amino fluorene	8.3	H ₂ SO ₄ , 70 mg.	110	97	3.10	2.55		Decomposition
69	9-Dimethylamino fluorene	9.5	—	110	97	3.17	2.46		Decomposition
70	9-Dimethylamino fluorene	9.5	NaOH, 1 mg.	110	97	3.17	2.64		Decomposition
71	9-Dimethylamino fluorene	9.5	H ₂ SO ₄ , 70 mg.	110	96	3.17	2.45		Decomposition

number ranging from 1.9 to 2.0, and which were therefore not quite decisive on the question as to whether two or three hydrogens are involved. The exchange of indene has been reinvestigated by Eberly,⁹ working with indene samples which have been more highly purified and with sodium ethylate as a catalyst, and he has obtained the value 2.5 for the exchange number, which is in accord with a value of three for the number of exchangeable hydrogen atoms.

Our study of compounds of this type has been extended to include a number of derivatives of fluorene in which the substituents occupy the 9 position. The results are tabulated in Table II. 9-Fluorenol, as might be expected, exchanges one hydrogen in neutral solution. In alkaline solution a second hydrogen atom exchanges, presumably the hydrogen atom at the 9 position. In acid solutions of comparable strength the compound decomposes rapidly, forming dibiphenyleneethylene. 9-Methoxyfluorene also decomposes in acid solution, but, in contrast to the behavior of 9-fluorenol, no exchange was observed in either neutral or alkaline solution. Thus, while the presence of a hydroxyl group appears to have no very marked effect on the lability of the remaining hydrogen atom on the 9 position, a methoxy group has a very pronounced inhibiting effect. The corresponding 9-amino and 9-dimethylamino compounds were investigated but it was found that these substances decomposed in both neutral and alkaline solutions, as well as in acid solution, the decomposition product being in each instance dibiphenyleneethane.

In connection with the supposed steric hindrance in the reactions of acetomesitylene, we have been interested in comparing the hydrogen exchange of this substance with acetophenone. It is to be expected that the exchange reactions of these ketones, like enolization reactions, would be subject to catalysis by both acids and bases. This type of behavior has been observed previously in the exchange reactions of acetone and cyclohexanone. The experimental results for acetophenone and acetomesitylene are included in Table II, and it is evident that these reactions are also subject to catalysis by both acids and bases. The exchange reaction of mesitylene takes place to a greater extent than the corresponding reaction of acetophenone, the difference being particularly noticeable in neutral solution where, under the experimental conditions adopted, the acetomesitylene exchange is about 50 per cent. complete while the exchange of acetophenone is about 5 per cent. complete. These results indicate that the process of enolization in acetomesitylene, whether acid- or base-catalyzed, is appreciably faster than in acetophenone. Kohler and Baltzly¹⁰, in a study of the reactions of acetomesitylene, came to the con-

⁹ EBERLEY, Doctor's Dissertation, University of Chicago, 1938.

¹⁰ KOHLER AND BALTZLY, *J. Am. Chem. Soc.*, **54**, 4015 (1932).

clusion that the failure of this substance to exhibit the normal addition reactions of ketones is due to steric hindrance and not to a greater tendency toward enolization for which they could find no evidence. Our results do not necessarily invalidate their conclusion, but we prefer to regard the lower reactivity of acetomesitylene in carbonyl addition reactions, as well as its greater tendency toward enolization, as an effect due, in part at least, to the higher electronegativity of the mesityl radical as compared with the phenyl radical.

We include also in this report some further experiments on quinaldine. It was previously reported¹ that at 110° for 60 hours this substance exhibited exchange almost to the extent of three hydrogens. The lability of the methyl hydrogens in quinoline and related compounds is well known, and it could be anticipated on general chemical grounds that these hydrogens would be exchangeable under the influence of either acidic or basic catalysts. The occurrence of exchange without an added catalyst might indicate either that the base strength of quinoline is sufficient for a self-catalyzed exchange reaction or, in view of the probable high sensitivity of the substance to acid catalysis that the reaction mixture contained sufficient acid as an impurity to promote the reaction. On repeating the experiment with the latter possibility in mind, we have confirmed the previous result with regard to the occurrence of a reaction without added catalyst, but not with regard to the extent of the reaction. The exchange now observed at 110° for 106 hours corresponds to the exchange of somewhat less than one hydrogen. That the reaction is subject to acid catalysis is shown by the results from experiments carried out at room temperature. Here in the absence of added catalyst no exchange occurs, but when a relatively small amount of sulfuric acid is added exchange takes place.

EXPERIMENTAL RESULTS

The experimental procedure has been, as before, to prepare mixtures of the substance under investigation, deuterioalcohol, and the catalyst, in evacuated tubes which were then sealed and placed in a thermostat for a specified period of time. At the end of this period the tubes were re-attached to the vacuum line, the break-seals opened, and the alcohol recovered from the mixtures by vacuum distillation. The deuterium content of the alcohol samples was determined by density measurements on water formed in the combustion of the alcohol.

Some improvements have been made in the analytical procedure, particularly in the procedure for the combustion of the alcohol samples. The combustion was originally carried out using a small alcohol lamp operating in a stream of dry air and adjusted to give a blue flame. The resulting gas was passed over a heated copper oxide catalyst to complete the combustion and then through a cooled trap where the water was collected. In

the present work the alcohol lamp was retained, but with the substitution of a sintered glass wick for the original asbestos wick, and the copper oxide catalyst was replaced by a platinum catalyst supported on a granular fused quartz. These changes were made with a view toward reducing errors caused by contamination of the sample by adsorbed water. The sequence of operations in the purification of the water samples has been altered by including a period of heating with freshly precipitated silver oxide subsequent to distillation from alkaline permanganate. As a result of these changes it has been possible to reduce the analytical errors to about half their former magnitude. The errors have been rendered still less signifi-

TABLE III
EXCHANGE REACTIONS OF ADDITIONAL SUBSTANCES

REF. NO.	SUBSTANCE	M-MOLES.	CATALYST	TEMP., °C.	TIME HRS.	INITIAL D ₂ O	FINAL D ₂ O	EXCH. NO.
109	Acetophenone	42.6		110	97	3.00	2.81	0.14
114	Acetophenone	42.6	NaOH, 2 mg.	110	96	3.00	1.45	2.15
111	Acetophenone	42.6	H ₂ SO ₄ , 140 mg.	110	112	3.00	1.64	1.63
88	Acetomesitylene	29.8		110	96	3.17	2.24	1.20
89 ^a	Acetomesitylene	29.8	NaOH, 2 mg.	110	97	3.17	1.70	2.49
91	Acetomesitylene	29.8	H ₂ SO ₄ , 140 mg.	110	97	3.17	1.80	2.10
16	Quinaldine	36.3		110	96	3.43	2.67	0.67
36	Quinaldine	36.3		25	24	3.10	2.98	0.09
50	Quinaldine	36.3		25	167	3.10	3.01	0.07
51	Quinaldine	36.3	H ₂ SO ₄ , 140 mg.	25	24	3.10	2.68	0.29
66 ^b	Styrene	45.2		110	100	3.17	2.39	0.62
67 ^c	Styrene	45.2	NaOH, 2 mg.	110	97	3.17	2.67	0.28
65 ^c	Styrene	45.2	H ₂ SO ₄ , 140 mg.	110	106	3.17	2.83	0.17

^a Exchange 3H's.

^b Some polymerization.

^c Extensive polymerization.

cant by the use of alcohol of higher deuterium content. In the determination of the deuterium content of water samples by the float-temperature method, the floating temperature was observed with a thermometer reading directly to 0.1° and permitting estimation to within 0.01°.

The extent of the exchange reaction is indicated in the tables of results (Tables I-III) under the heading of "exchange number." This is calculated from the experimental data by means of the following equation:

$$n = \frac{a}{s} \left(\frac{D_1}{D_2} - 1 \right)$$

where n is the exchange number, s is the number of moles of substance, a is the number of moles of alcohol, and D_1 and D_2 represent the initial and final concentrations of deuterium in the alcohol.

In an idealized case, namely one in which equilibrium has been established, and in which the partition coefficient for the distribution of deuterium is equal to unity, the exchange number, as defined by the above equation, would be equal to the number of hydrogen atoms per molecule taking part in the exchange reaction. Actually the distribution of deuterium is not a purely statistical one, and fractional values for the exchange numbers are to be expected. In exchange reactions involving C—H hydrogens the deviations are such that the deuterium shows a slight preference for the alcoholic linkage and in such cases the observed exchange numbers are less than the theoretical values for the number of exchangeable hydrogen atoms. These effects can be interpreted, qualitatively at least, on the basis of the differences in zero-point energies of vibration.

In the tables of results the deuterium concentrations given are the concentrations of deuterium in the water samples (as D_2O , in mole per cent.) formed in the combustions. The values were obtained directly from the calibration curve for the quartz float, and since only the ratio of initial to final concentrations enters into the calculation of the exchange number it is not necessary to convert the D_2O concentrations to C_2H_5OD concentrations.

Small corrections were applied in the calculation of the exchange numbers for the exchange reactions of dimethylaniline derivatives catalyzed by sulfuric acid, the correction being necessitated by the dilution of the deuterioalcohol by the light hydrogen of the sulfuric acid. These corrections were not applied to the corresponding data for diphenylamine and triphenylamine, as some uncertainty existed as to whether it should be applied. In the former cases the alcohol recovered from the reaction mixtures was treated with phosphorous pentoxide, primarily to remove traces of amines, but this treatment also served to remove water. In the experiments on diphenylamine and triphenylamine the alcohol was not so treated and could have contained an amount of water equivalent to the amount of sulfuric acid originally added. This would result in an increased concentration of deuterium in the water of combustion and hence introduce an error opposite in direction to that caused by the dilution of the deuterioalcohol with sulfuric acid.

MATERIALS

Deuteroalcohol.—Deuteroalcohol was prepared, as in the previous work by means of the rapid exchange reaction between ethyl alcohol and deuterium oxide. After mixing absolute alcohol and the desired quantity of deuterium oxide, the alcohol was dried by repeated treatments with freshly ignited calcium oxide. The proportions of alcohol to deuterium oxide were chosen so as to yield a product containing approximately 20 mole per cent. C_2H_5OD .

Dimethylaniline.—Commercial dimethylaniline was twice distilled over sodium, a fraction, b.p. 190–192°, being collected on the second distillation.

Diphenylamine.—Recrystallized from ethyl acetate, decolorized in hot alcoholic solution with Norite, distilled three times at 6 mm. pressure, m.p. 54°–55°.

Triphenylamine.—Purified by vacuum distillation, m.p. 126.5°.

p-Nitrodimethylaniline.—From *p*-nitroaniline on methylation with dimethyl sulfate. Product purified according to the method of Davies¹¹ m.p. 162°.

m-Nitrodimethylaniline.—By the nitration of dimethylaniline according to the method of Nölting and Faurneau¹². Purified by vacuum distillation and recrystallizations from alcohol, yielding a product of constant melting point, 61° (literature, 66°).

m-Bromodimethylaniline.—This compound was prepared in 15% yield by the action of dimethyl sulfate on *m*-bromoaniline¹³. The product reacted very slightly with acetyl chloride and may therefore have been contaminated with the monomethyl derivative. The erratic experimental results for the hydrogen exchange in neutral solution likewise indicate that the compound was not of satisfactory purity, but these results could not be accounted for by the presence of the monomethyl compound. The fact that no exchange occurred when a small amount of sodium hydroxide had been added (expt. 53) suggests that the observed exchange in neutral solution (expts. 54, 75) was a result of catalysis by an acidic impurity.

o-Nitrodimethylaniline.—Samples prepared by the methylation of *o*-nitroaniline with dimethyl sulfate were unsatisfactory because of contamination by the monomethyl derivative. A satisfactory product was obtained by the action of dimethylaniline on *o*-chloronitrobenzene¹⁴. Red oil; b.p. 157–158°/20 mm.

Fluorene.—Purified by repeated recrystallization from alcohol, m.p. 112°.

9-Fluorenol.—Prepared from fluorenone by reduction with zinc dust and ammonia¹⁵. The product was isolated from the reaction mixture by extraction with alcohol, and after several recrystallizations from alcohol was sublimed *in vacuo*, m.p. 152°.

The decomposition of fluorenol under the influence of sulfuric acid (expt. no. 39) resulted in the formation of an orange solid, m.p. 186–191°, probably dibiphenyleneethylene (m.p. 189–190°). In expt. 93, in which fluorenol was treated in solution in deuterioalcohol with a relatively large amount of sodium hydroxide (1 mole) the solution became deep red in color, and from it was isolated a pale yellow solid, m.p. 116°, probably fluorene.

9-Methoxyfluorene.—From 9-chlorofluorene on treatment with silver nitrate in methyl alcohol solution. After separation of the silver chloride precipitate by filtration, the alcohol was evaporated, and the product taken up in ligroin, from which it was obtained in large yellow crystals, m.p. 41° (literature, 43°); mol. wt. (in cyclopentadecanone), found 192, calc'd 196. The color of this material was probably due to traces of dibiphenyleneethylene. In the exchange experiments on this substance, no decomposition occurred in neutral or alkaline solution, but extensive decomposition occurred in acid solution. The product was a solid insoluble in alcohol and in ligroin; it decomposes gradually on heating above 145°.

9-Aminofluorene.—By reduction of fluorenone oxime by zinc dust in acetic acid¹⁶.

¹¹ DAVIES, *Bull. soc. chim.*, [5], 2, 295–96 (1935).

¹² NÖLTING AND FOURNEAU, *Ber.*, 30, 2931 (1897).

¹³ KHARASCH AND PICCARD, *J. Am. Chem. Soc.*, 42, 1855 (1920).

¹⁴ LEFEVRE, *J. Chem. Soc.*, 1930, 149.

¹⁵ WERNER AND GROB, *Ber.*, 37, 2895 (1904).

¹⁶ INGOLD AND WILSON, *J. Chem. Soc.*, 1933, 1499.

The product was purified by extraction with ligroin in a closed system, and was obtained on evaporation of the ligroin as light-brown crystals, m.p. 63°.

The product of the decomposition of α -aminofluorene in neutral solution was a colorless solid, m.p. 231–235°; mol. wt. found 335, calc'd for dibiphenyleneethane, 330. *Anal.*: found, C, 94, 21; H, 6.06; calc'd for dibiphenyleneethane, C, 94.6; H, 5.4. The decomposition in acid solution (expt. 59) yielded a similar product, m.p. 240°, while the decomposition in the presence of alkali (expt. 58) yielded an impure material, m.p. 175–185°.

9-Dimethylaminofluorene.—From 9-aminofluorene hydrochloride on treatment with methyl alcohol at 115° for 96 hours in sealed tubes. Recrystallized from ligroin, m.p. 54°; recorded melting point 49°. The crystals, originally colorless, became greenish on keeping. The materials recovered from the exchange reaction mixtures were similar to those obtained with 9-aminofluorene and probably consisted chiefly of dibiphenyleneethane.

Acetomesitylene.—From mesitylene and acetyl chloride¹⁷; b.p. 156°/53 mm.

Quinaldine.—Purified by multiple vacuum distillation; b.p. 244.5°.

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SUMMARY

1. Previous discussion of the probable mechanism of certain hydrogen-deuterium exchange reactions has been amplified and extended.
2. Preliminary experimental results previously reported have been re-checked and supplemented.
3. Further experimental implications of the mechanism postulated have been pointed out.
4. The results of additional experiments are reported and are shown to be consistent with the mechanism proposed.
5. An ortho effect appears in the hydrogen-deuterium exchange reactions of ortho-substituted dimethylanilines. A tentative explanation has been advanced.

¹⁷ GILMAN, "Organic Syntheses," Coll. vol. I., John Wiley and Sons, 1925, p. 334.

